PATENT
Docket No. 6283.NCP2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Stockman et al.
Serial No.: 10/044,219
Confirmation No.: 9179
Filed: November 19, 2001
For: METHODS FOR CREATING A COMPOUND LIBRARY

Group Art Unit: 1627
Examiner: Unknown

OFFICIAL

pre b/a
Suggs
7-16-02

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
ATTN: BOX PATENT APPLICATION
Washington, D.C. 20231

Dear Sir:

The present application is a continuation-in-part of patent application of Serial No. 09/677,107 filed on September 29, 2000.

Prior to taking up the above-identified application for examination, please amend the application as follows:

In the Specification

Please replace the paragraph beginning at **page 23, line 10**, with the following rewritten paragraph. Per 37 C.F.R. §1.121, this paragraph is also shown in Appendix A with notations to indicate the changes made.

Changes in chemical shifts, relaxation properties or diffusion coefficients that occur upon the interaction between a protein and a small molecule have been documented for many years (for recent reviews see M. J. Shapiro et al., *Curr. Opin. Drug. Disc. Dev.*, **2**, 396 (1999); J. M. Moore, *Biopolymers*, **51**, 221 (1999); and B. J. Stockman, *Prog. NMR Spectr.*, **33**, 109 (1998)).

A1

Observables typically used to detect or monitor the interactions are chemical shift changes for the ligand or isotopically-enriched protein resonances (J. Wang et al., *Biochemistry*, **31**, 921 (1992)), or line broadening (D. L. Rabenstein, et al., *J. Magn. Reson.*, **34**, 669 (1979); and T. Scherf et al., *Biophys. J.*, **64**, 754 (1993)), change in sign of the NOE from positive to negative (P. Balaram et al., *J. Am. Chem. Soc.*, **94**, 4017 (1972); and A. A. Bothner-By et al., *Ann. NY Acad. Sci.* **222**, 668 (1973)), or restricted diffusion (A. J. Lennon et al., *Biophys., J.* **67**, 2096 (1994)) for the ligand. For the most part, these studies have focussed on protein/ligand systems where the small molecule was already known to be a ligand or was assumed to be one. In the last several years, however, the work of the Fesik (S. B. Shuker et al., *Science*, **274**, 1531 (1996); and P. J. Hajduk et al., *J. Am. Chem. Soc.*, **119**, 12257 (1997)), Meyer (B. Meyer et al., *Eur. J. Biochem.*, **246**, 705 (1997)), Moore (J. Fejzo et al., *Chem. Biol.*, **6**, 755 (1999)), Shapiro (M. Lin et al., *J. Org. Chem.*, **62**, 8930 (1997)), and Dalvit (C. Dalvit et al., *J. Biomol NMR*, **18**, 65-68 (2000)) labs has demonstrated the applicability of these same general methods as a screening tool to identify ligands from mixtures of small molecules.